

WHAT IS CLAIMED IS:

1. A conjugate, comprising a targeted agent and a chemokine receptor targeting agent, or a portion thereof, wherein the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

2. A conjugate of claim 1, comprising the following components: (chemokine receptor targeting agent)_n, (L)_q and (targeted agent)_m, wherein:

L is a linker for linking the chemokine receptor targeting agent to a targeted agent;

chemokine receptor targeting agent is any moiety that selectively binds to a chemokine receptor;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents the targeting agents are the same or different.

3. The conjugate of claim 2, wherein m and n, which are selected independently, are 1-6.

4. The conjugate of claim 2, wherein q is 1, n is 2 and m is 1.

5. The conjugate of claim 1, wherein the chemokine receptor targeting agent is a chemokine, an antibody that specifically binds to a chemokine receptor or a fragment of the chemokine or antibody, wherein the fragment binds to the receptor and internalizes the targeted agent.

6. The conjugate of claim 1, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on activated leukocytes.

5 7. The conjugate of claim 1, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on cells selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

10 8. The conjugate of claim 6, wherein the leukocytes are selected basophils, neutrophils, eosinophils, and combinations of any two or more thereof.

9. The conjugate of claim 1, wherein the targeted agent is a toxin, a nucleic acid or a therapeutic protein.

15 10. The conjugate of claim 1, wherein the chemokine receptor targeting agent and targeted agent are linked directly via a covalent or ionic linkage.

11. The conjugate of claim 1, wherein the chemokine receptor targeting agent and targeting agent are joined via a linker.

12. The conjugate of claim 24, wherein the linker is a peptide linkage, a polypeptide or is chemical linker.

20 13. The conjugate of claim 25, wherein the linker is a peptide or an amino acid

25 14. The conjugate of claim 1, further comprising a non-chemokine cytokine or a receptor associated protein that binds to receptors on and/or activates one or more of the cells that promote secondary tissue damage, other than chemokine receptors.

15. The conjugate of claim 14, wherein the cytokine binds to a cytokine-specific receptor expressed on cells that express chemokine receptors.

16. The conjugate of claim 14, wherein the cytokine is selected from among interleukins, lymphokines, monokines, colony-stimulating factors and receptor associated proteins.

17. The conjugate of claim 1, wherein the chemokine receptor
5 targeting agent is a monoclonal antibody, or an antigen-specific fragment thereof.

18. The conjugate of claim 1, further comprising an antibody that binds to a non-chemokine cytokine receptor and/or to a non-chemokine cytokine.

10 19. A nucleic acid molecule, comprising a sequence of nucleotides encoding a conjugate of claim 1.

20. The nucleic acid claim 19 that is DNA.

21. A plasmid, comprising the nucleic acid molecule of claim 19.

22. A host cell, comprising the plasmid of claim 21.

15 23. A method of producing a conjugate, comprising culturing the cell of claim 21 under conditions, whereby a fusion protein comprising the conjugate is expressed, and isolating the fusion protein.

24. A pharmaceutical composition comprising a therapeutically effective concentration or amount of a conjugate of claim 1 in a
20 pharmaceutically acceptable vehicle.

25. A method for treating disorders associated with inflammatory responses related to activation, proliferation and migration of immune effector cells, comprising administering a conjugate that comprises a non-chemokine cytokine and a targeted agent, whereby
25 inflammatory responses associated with activation, proliferation and/or migration of the immune effector cells is inhibited, wherein:

the cytokine specifically binds to the immune effector cells, and upon binding internalizes a linked targeted agent; and

the targeted agent inhibits activation, proliferation or migration of the immune effector cell.

26. The method of claim 25, wherein the immune effector cells are leukocytes that express chemokine receptors.

5 27. The method of claim 25, wherein the inflammatory response results in secondary tissue damage.

28. The method of claim 25, wherein the cells are selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

10 29. A method for treating inflammatory responses associated with activation, proliferation and migration of immune effector cells, comprising administering a conjugate of claim 1 to an animal mammal, whereby an inflammatory response associated with activation, proliferation migration or the immune effector cells is inhibited.

15 30. The method of claim 29, wherein the disorder or disease state comprises secondary tissue damage.

31. The method of claims 29, wherein the disorder or disease state is selected from the group consisting of CNS injury, CNS inflammatory diseases, neurodegenerative disorders, heart disease, inflammatory eye diseases, inflammatory bowel diseases, inflammatory joint diseases, inflammatory kidney or renal diseases, inflammatory lung diseases, inflammatory nasal diseases, inflammatory thyroid diseases, bacterial or viral infections and cytokine-regulated cancers.

20 32. The method of claim 31, wherein the CNS inflammatory diseases and neurodegenerative disorders are selected from the group consisting of stroke, closed head injury, leukoencephalopathy, choriomeningitis, meningitis, adrenoleukodystrophy, AIDS dementia complex, Alzheimers disease, Down's Syndrome, chronic fatigue syndrome, encephalitis, encephalomyelitis, spongiform encephalopathies,

multiple sclerosis, Parkinson's disease, and spinal cord injury/trauma (SCI).

33. The method of any of claim 29, wherein the chemokine receptor targeting agent is a chemokine.

34. The method of claim 29, wherein the targeted agent is a toxin.

35. A method of targeted delivery of an agent into cells that express chemokine receptors, comprising associating the agent with a chemokine receptor targeting agent, whereby the agent is internalized by the cells.

36. The method of claim 35, wherein the cells are activated leukocytes.

37. The method of claim 27, wherein the secondary tissue damage results from spinal cord injury or trauma.

38. A method of inhibiting proliferation, migration or activation of cells bearing chemokine receptors, comprising contacting the cells with an effective amount of a conjugate of claim 1.

39. A method of effecting gene therapy, comprising contacting cells bearing chemokine receptors with the conjugate of claim 1, wherein the targeted agent is a nucleic acid.

40. A method for treating secondary tissue damage and associated disease states, comprising administering to a subject in need thereof an effective amount of a therapeutic agent that inhibits the proliferation, migration or physiological activity of secondary tissue damage-promoting cells.

41. A conjugate of claim 1 selected among OPL98104, OPL98112, OPL98108, OPL98102, OPL98110, OPL98106, OPL98101, OPL98109, OPL98105, OPL98103, OPL98111 and OPL98107.